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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,406	06/24/2003	Pier Andrea Borea	PAT-0040-US-NP2	4184

57999 7590 08/28/2008

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	**PAPER NUMBER**
1618	
MAIL DATE	**DELIVERY MODE**
08/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/603,406	BOREA ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,8,11-16,19 and 28-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,8,11-16,19 and 28-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed **2/28/08** presents remarks and arguments to the office action mailed **11/29/07**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of Action

Claims 7-8, 11-16, 19 and 28-42 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-8, 11-16, 19 and 28-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite using the term "**countering**" but fail to define the metes and bounds of the term. What is meant by the term "countering"? The specification (pages 6-8) fails to describe any supportive definition to the term "countering" in the claims.

The claims must be clearly and distinctly describe the claim invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Claims 7-8, 11-14, 16, 19, 28-29, 31-33, 35, 37-38,40 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Leung et al. (US 6,326,390 B1; IDS reference AD 1/12/04).

Leung discloses with regard to instant claim 7, a method of inhibiting tumor growth by the administration of adenosine A_3 antagonists to a patient either alone or in combination with other anti- tumor agents, such as anti-angiogenic agents and/or cytotoxic agents (abstract) in the treatment of solid tumors wherein the tumor is breast cancer, prostrate cancer (claims 11 and 32) (see column 6, line 39). And the A_3 receptor antagonist is MRE-3008F20 (claims 7, 19, 33, 38) (see compound 1; column 4, lines 27-29). And the chemotherapeutic agents such as doxorubicin, vinca alkaloid and docetaxel (see column 5, lines 65) (as in claims 13-14 and 28-29, 35, 37, 40 and 42). Claims 8 and 19 are also anticipated wherein R^2 in the compound is MRE-3008F20 is an alkyl. Breast cancer is a multi-drug resistant cancer and will inherently have P-

glycoprotein....as evidence by Alexis (multidrug resistance 12/2001), therefore claim 12 is anticipated. The reference also teaches the drugs of the reference can be combined with antibiotics as required by instant claims16, 31. Applicant's recitation of a new mechanism of action such as "countering" for the prior art method will not by itself distinguish the instant claims over the prior art teaching of the same or nearly the same method step which is administering. Note that a mechanism of action of treatment would not by itself carry patentability weight if the prior art teaches the same or nearly the same method step. In the instant case the same method step is disclosed in the reference, administering the same compound will inherently have the same mechanism.

Maintained Claim Rejections - 35 USC § 103 revised with new claims

Claims 7-8, 11-16, 19 and 28-42 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,210,917 to Carson et al. in view of Jacobson et al. US Patent No. 6,066,642 and further in view of Baraldi et al., Journal of Medicinal Chemistry. Vol. 42 (1999) 4473-4478 (all of record) and Goodman and Gilman, The pharmacological Basis of Therapeutics (of record).

Applicant argues that (i) Carson et al. does not teach or suggest a therapy comprising adenosine-5'-triphosphate when taken alone or in combination with other references that the A3 receptor antagonist could be employed to inhibit P-glycoprotein and multidrug resistance associated with protein mediated drug reflux in cancer. That the teaching of Carson et al is to depriving the cancer cells of the energy required to maintain P-gp mediated resistance.

Applicant further argues that (ii) Jacobson et al. uses the A_3 receptor antagonist in killing cancer cells wherein the A_3 receptor maybe used alone or in combination with other pharmaceutically active compounds. Applicant argues that the teaching does not show clear evidence whether an adenosine A_3 receptor agonist or antagonist should be used in the treatment of diseases such as cancer. That Fishman et al. teaches away from the methods of the instant invention.

Baraldi et al. teaches MRE3008F20 compound which is an adenosine A_3 receptor antagonist, and that Goodman and Gilman teaches local means of therapy.

In summary Applicant argues that none of the references cited in the office action of record teaches the countering effect and the synergistic effect of the combination therapy. Applicant again relies upon unexpected result to overcome the rejection.

In response, with regard to (i) Carson does not need to have recognized the same property for a 103 rejection, all it needs is the reasonable expectation of success in treatment of the claimed method. Carson et al. teaches that MDR can be overcome in certain cancer cells by application of an inhibitor of de-novo adenine synthesis, that cancer cells are treated with combination of chemotherapeutic agents and purine synthesis inhibitors. Please see col. 2, lines 15-17 and lines 35-40 of the '917 reference. Thus one of ordinary skill in the art would have been motivated to use a purine synthesis inhibitor with a chemotherapeutic drug for the countering of MDR as taught.

Next, Applicant correctly acknowledges that Jacobson et al. teach the use of adenosine A3 receptor antagonist in killing of cancer cells wherein the A_3 antagonist

maybe used alone or in combination. Clear evidence as alleged by Applicant is not the standard for obviousness. Applicant states that Fishman et al. teaches away from the methods of the instant invention. Teaching away would require that the agonist is not useful. Less preferred embodiment such as, the agonist is not teaching away. It does however teach that the compounds may be useful in cancer treatment.

With regard to the showing of unexpected result, careful consideration has been given however, the results are not commensurate in scope with the claims. Claim 7, for example recites administering the A_3 antagonist either prior to administering the chemotherapeutic drug or after. There is no showing of how synergism is accomplished when the drug is applied prior to the chemotherapeutic agent. How does administering the drug 10 days or a year before administering the chemotherapeutic agent yield synergism? The showings are to a cell culture, wherein the combination is used together.

Also, Applicant's recitation of a new mechanism of action such as "countering" for the prior art method will not by itself distinguish the instant claims over the prior art teaching of the same or nearly the same method step which is administering. Note that a mechanism of action of treatment would not by itself carry patentability weight if the prior art teaches the same or nearly the same method step. In the instant case the same method step is disclosed in the reference, administering the same compound will inherently have the same mechanism.

Careful consideration has been given to the unexpected results; however, the results fail to show a trend with the claimed invention because the unexpected result

should be commensurate in scope with the claims. The claims recite the administration of A3 receptor antagonist either prior to or during administration of the chemotherapeutic cancer agent. The data does not provide administration of the chemotherapeutic cancer agent before the A3 receptor. A specific concentration of the A3 receptor antagonist is shown to be synergistic with a specific concentration of specific chemotherapeutic cancer agents that are not in the claims, therefore the data provided is not commensurate with the claims.

No claim is allowed

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

SVG
6/24/08